UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,083	09/09/2003	Simon Delagrave	20446-002001 / BTS0001-10	2730

26161 7590 08/07/2007
FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
STEELE, AMBER D	
ART UNIT	**PAPER NUMBER**
1639	
MAIL DATE	**DELIVERY MODE**
08/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/659,083	DELAGRAVE, SIMON	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-69* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The non-responsive amendment received on January 16, 2007 canceled claims 3-50, amended claim 1, and added new claims 51-60.

The amendment to the claims received on June 4, 2007 canceled all pending claims (i.e. claims 1-60) and added new claims 61-69.

Claims 61-69 are currently pending and under consideration.

Election/Restrictions

2. Applicant elected (with traverse) Group I (original claims 1-12, now claims 61-69) in the reply filed on April 20, 2006. The requirement was deemed proper and made FINAL in the Office action mailed on September 28, 2006.

3. Due to the claim amendments received on June 4, 2007 which clarify the presently claimed method, the species requirement is withdrawn.

Priority

4. The present application claims benefit of U.S. application 60/416,819 filed October 8, 2002.

Invention as Claimed

5. A method of countering the development of resistance in a parent target to a parent neutralizing agent wherein the parent neutralizing agent neutralizes the parent target comprising coevolving said parent target and said parent neutralizing agent wherein said coevolving comprises: (a) diversifying said parent target and said parent neutralizing agent, (b) selecting one or more next generation neutralizing agents and next generation targets form diversified populations resulting from said diversifying wherein the selected one or more neutralizing agents and targets have improved neutralizing activity and resistance, and (c) optionally repeating said diversifying and selecting using said one to more next generation neutralizing agents or next generation targets wherein the improved neutralizing activity of the neutralizing agent counters the improved resistance of the parent target thereby countering the development of resistance and variations thereof.

Applicant's Definition of Relevant Terms

6. Neutralizing agent refers to any entity capable of wholly or partially neutralizing at least one activity of a target including binding. Please refer to the present specification paragraph 27.

Neutralizing activity refers to the ability of a neutralizing agent to counter or deactivate at least one activity of a target. For example, neutralizing activity can be an ability to antagonize a target such as by lessening the target's ability to perform at least one of its functions including binding to the neutralizing agent. Please refer to the present specification paragraph 28.

Resistance refers to the ability of a target to thwart or withstand the neutralizing activity of a neutralizing agent. Please refer to the present specification paragraph 31.

Withdrawn Objection

7. The objection to claim 1 is moot due to the cancellation of the claim 1 in the claim amendments received on June 4, 2007.

Withdrawn Rejections

8. The rejection of claims 1-3, 5-6, and 8-12 under 35 U.S.C. 112, first paragraph (written description) is withdrawn in view of the claim amendments received on June 4, 2007 clarifying the claimed method of countering the development of resistance.

9. The rejection of claims 1-3, 5-6, and 9-12 under 35 U.S.C. 102(e) as being anticipated by McCafferty et al. U.S. Patent 6,916,605 is withdrawn due to the claim amendments received on June 4, 2007.

Maintained Rejection

10. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Please note: the rejections have been altered to reflect the claim amendments received on June 4, 2007.

Claim Rejections - 35 USC § 102

11. Claims 61-64 and 66-69 are rejected under 35 U.S.C. 102(b) as being anticipated by Karrer et al. WO01/32712 A2 published May 10, 2001.

For present claim 61, Karrer et al. teach methods of improving antibodies via in vitro coevolution of an antibody and the cognate antigen wherein the antibody and/or antigen is

selected for a desirable trait or property including increased affinity, decreased undesirable side-effects, increased avidity, broad neutralizing activity, and enhanced function including overcoming resistance (please refer to page 70, lines 10-12) wherein the initial antibody can be a known antibody (i.e. known neutralizing activity) via diversifying, selecting for a desired trait or property, and repeating (please refer to entire specification particularly abstract; pages 1-38 and 68-98; Tables 1, 2A, 2B). In addition, Karrer et al. teach improving neutralization of bacterial enterotoxins (i.e. countering resistance via improving neutralizing activity; please refer to pages 17-19).

For present claim 62, Karrer et al. teach mutagenesis (please refer to entire specification particularly pages 17-34 and 70-89).

For present claim 63, Karrer et al. teach multiple rounds of diversification and selecting altered antibodies and/or antigens between the rounds of diversification until the desired outcome is obtained including broad affinity and broad neutralizing activity (e.g. repeating for broad neutralizing activity; please refer to entire specification particularly pages 6, 17, 28, 31, 82, 85-87).

For present claim 64, Karrer et al. teach proteins including antibodies, antigens, etc. (please refer to entire specification particularly pages 6-8, 11-13, 17-20, 28, 31-32, 34-38, 68-73, 85-87).

For present claim 66, Karrer et al. teach antibodies as neutralizing agents (please refer to entire specification particularly pages 6-8, 11-13, 17-20, 28, 31-32, 34-38, 68-73, 85-87).

For present claim 67, Karrer et al. teach antigens as targets (please refer to entire specification particularly pages 6-8, 11-13, 17-20, 28, 31-32, 34-38, 68-73, 85-87).

For present claim 68, Karrer et al. teach viruses including HIV (please refer to entire specification particularly abstract and pages 6-8, 11-13, 17-20, 28, 31-32, 34-38, 68-73; 85-87).

For present claim 69, Karrer et al. teach antibodies to viruses including RSV (e.g. Synagis®; please refer to entire specification particularly pages 63-65).

Therefore, the presently claimed invention is anticipated by the teachings of Karrer et al.

Arguments and Response

12. Applicant's arguments directed to the rejection under 35 USC 102 (b) as being anticipated by Karrer et al. WO01/32712 A2 for claims 61-64 and 66-69 were considered but are not persuasive for the following reasons.

Applicant contends that Karrer et al. do not teach each limitation of the claims. Specifically, applicant states that Karrer et al. do not teach utilizing agents with a previously known neutralizing activity, countering the development of resistance, selecting next generation targets with improved resistance to the parent neutralizing agent, PDZ, or RSV.

Applicants' arguments are not convincing since the teachings of Karrer et al. anticipate the method of the instant claims. Karrer et al. teach that the initial antibody can be a known antibody with a known "neutralizing" activity (e.g. binding to target to alter any function of the target), resistance to a pathogenic challenge can be used to select antibodies with enhanced functions, multiple rounds of selection for desirable traits of properties including properties related to resistance, and RSV (please refer to the entire specification particularly page 6, particularly lines 1-2 and 28-32; Tables 1-2B particularly pages 63-65 regarding RSV antibodies; page 70, lines 10-12). The examiner of record has not suggested that Karrer et al. teach PDZ containing neutralizing agents.

New Rejections Necessitated by Amendment

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 61-64 and 68 are rejected under 35 U.S.C. 102(b) as being anticipated by Rosin et al. PNAS 96: 1369-1374, 1999(supplied in IDS received on 11/13/03).

For present claim 61, Rosin et al. teach coevolution of resistance-evading peptidomimetic inhibitors of HIV-1 protease comprising providing HIV-1 protease (i.e. diversified parent target via naturally occurring mutants or computationally designed) and computationally designed protease inhibitors (i.e. diversified parent neutralizing agent) and selecting resistance-evading protease inhibitors (please refer to the entire reference particularly the abstract and Methods).

For present claim 62, Rosin et al. teach computational design of protease inhibitors and HIV-1 protease (i.e. combinatorial synthetic methods; please refer to the entire reference particularly the abstract and Methods).

For present claim 63, Rosin et al. teach protease inhibitors for an entire class of mutating targets (i.e. broad neutralizing activity; please refer to the entire reference particularly the introduction and Methods).

For present claim 64, Rosin et al. teach peptide based protease inhibitors (please refer to the entire reference particularly the abstract, Methods, Tables 1-2).

For present claim 68, Rosin et al. teach HIV-1 protease (please refer to the entire reference particularly the abstract and Methods).

Therefore, the presently claimed invention is anticipated by the teachings of Rosin et al.

15. Claims 61-63 and 67-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Eaton et al. U.S. 5,723,289 issued March 3, 1998.

For present claim 61, Eaton et al. teach methods of coevolution or parallel SELEX comprising providing a nucleic acid-reactant test mixture which facilitates a chemical reaction including binding (i.e. diversified neutralizing agent) and free reactants or targets (i.e. diversified parent target, contacting the mixture and reactants to allow binding, partitioning, dissociating, amplification (i.e. all part of selection step), and reiterating the steps through as many cycles as desired to yield highly specific high affinity nucleic acid ligands to the target molecule with desired characteristics (i.e. countering the development of resistance; please refer to the entire specification particularly abstract; Figure 1; columns 1-3, 5, 7-12, 17-18, 20-24).

For present claim 62, Eaton et al. teach mutagenesis and combinatorial methods (please refer to the entire specification particularly columns 3, 7-8, 11-17).

For present claim 63, Eaton et al. teach nucleic acids with a broad variety of physical and chemical interactions (i.e. broad neutralizing activity; please refer to the entire specification particularly column 2, lines 1-11).

For present claim 67, Eaton et al. teach antigen targets (please refer to the entire specification particularly column 10, lines 3-10; column 18, lines 22-30).

For present claim 68, Eaton et al. teach viral targets (please refer to the entire specification particularly column 10, lines 3-10; column 18, lines 22-30).

Therefore, the presently claimed invention is anticipated by the teachings of Eaton et al.

16. Claims 61-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Staudinger et al. J. Biol. Chem. 272(51): 32019-32024, 1997.

For present claim 61, Staudinger et al. teach methods of determining binding (i.e. neutralizing activity) and determining which domains are necessary for binding (i.e. resistance = non-binders) comprising providing PICK1 and PICK1 mutants (i.e. neutralizing agents), providing PCK and PCK mutants (i.e. targets), and selecting binders verses nonbinders (please refer to the entire specification particularly abstract; Experimental Procedures; Figures 1-6).

For present claim 62, Staudinger et al. teach mutagenesis (please refer to the entire specification particularly Experimental Procedures).

For present claim 63, Staudinger et al. teach PICK1 binding to more than one protein including PKCα and PKC7 (i.e. broad neutralizing activity; please refer to the entire specification particularly abstract; Figures 2-6).

For present claim 64, Staudinger et al. teach proteins including PICK1 (please refer to the entire specification particularly abstract).

For present claim 65, Staudinger et al. teach PDZ domain containing proteins (please refer to the entire specification particularly abstract).

Therefore, the presently claimed invention is anticipated by the teachings of Staudinger et al.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ADS
July 30, 2007

MARK L. SHIBUYA
PRIMARY EXAMINER